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REVIEW

High-magnification selection of spermatozoa prior to oocyte injection: confirmed and potential indications

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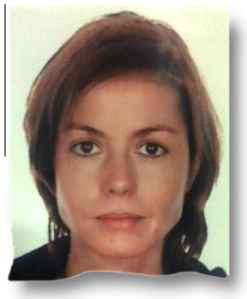

Florence Boitrelle, MD is working as an embryologist at Poissy General Hospital's assisted reproduction unit since 2009. She is currently working on her PhD thesis on the links between sperm morphology, nuclear quality, acrosome quality, genetics and epigenetics at the University of Versailles Saint-Quentin-en-Yvelines.

Abstract Intracytoplasmic morphologically selected sperm injection (IMSI) involves the use of differential interference contrast microscopy at high magnification (at least ×6300) to improve the observation of live human spermatozoa (particularly by showing sperm head vacuoles that are not necessarily seen at lower magnifications) prior to intracytoplasmic sperm injection (ICSI) into the oocyte. However, a decade after IMSI's introduction, the technique's indications and ability to increase pregnancy and/or birth rates (relative to conventional ICSI) are subject to debate. In an attempt to clarify this debate, this work performed a systematic literature review according to the PRISMA guidelines. The PubMed database was searched from 2001 onwards with the terms 'IMSI', 'MSOME' and 'high-magnification, sperm'. Out of 168 search results, 22 relevant studies reporting IMSI outcomes in terms of blastocyst, pregnancy, delivery and/or birth rates were selected and reviewed. The studies' methodologies and results are described and discussed herein. In view of the scarcity of head-to-head IMSI versus ICSI studies, the only confirmed indication for IMSI is recurrent implantation failure following ICSI. All other potential indications of IMSI require further investigation.

KEYWORDS: human spermatozoa, IMSI, MSOME, outcome, pregnancy rate, vacuole

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Introduction

Since its first use in the early 1990s (Palermo et al., 1992), intracytoplasmic sperm injection (ICSI) has become a powerful tool for infertile couples — particular in cases of severe male infertility and low sperm counts. In ICSI, the 'best-looking' live spermatozoon is chosen for its motility, viability and gross morphology, using Hoffman contrast microscopy and a magnification of ×200 or ×400. Although the fertilization and clinical pregnancy rates associated with ICSI are high (Palermo et al., 2009), it has been shown that ejaculate characteristics (e.g. normal spermatozoa or mild or severe oligoasthenoteratozoospermia) (Loutradi et al., 2006) and the morphology of the individually selected spermatozoon may affect post-ICSI fertilization, implantation and pregnancy rates (De Vos et al., 2003). These results can be explained (at least in part) by the fact that, even though a spermatozoon's morphology is slightly correlated with its chromatin condensation or DNA integrity, the selection of normal spermatozoa during ICSI does not enable spermatozoa with nuclear defects to be excluded (Abu Hassan Abu et al., 2012; Avendaño et al., 2009).

Hence, over the last decade, some researchers have tried to improve sperm observation with higher-resolution microscopy techniques. Their objective has been to establish correlations between the morphology of a viable (and subsequently injectable) spermatozoon and its inherent quality (in terms of chromosomal content, degree of chromatin condensation and/or DNA integrity). The most studied of these novel techniques is motile sperm organelle morphology examination (MSOME), which uses differential interferential contrast microscopy and high magnification (>×6300), first described by Bartoov et al. (2001). This observation technique reportedly enables better assessment of a spermatozoon's morphology and the visualization of sperm head vacuoles. The latter structures are not visible (particularly when they are small) at a conventional ICSI-like magnification (using Hoffman contrast and a magnification of ×200—×400) (Bartoov et al., 2001). Nevertheless, since the introduction of IMSI, more attention has been given to the pre-ICSI detection of spermatozoa that contain vacuoles. Over the last decade, many researchers have evaluated IMSI (i.e. the MSOME-based selection of a spermatozoon and then its injection into the oocyte) and compared it with the gold-standard technique, ICSI. However, IMSI's superiority over ICSI (in terms of pregnancy or delivery rates) is still subject to debate. The only meta-analysis of this topic was performed 3 years ago (Setti et al., 2010). It included three studies and, by pooling all the IMSI results, did not take account of the specific indication. In fact, the studies in this field differ significantly in terms of: (i) their design (e.g. randomized versus non-randomized studies, or the comparison of IMSI results with previous ICSI results for the same couples versus other couples matched according to various criteria); (ii) the ICSI magnification used; (iii) the sprm morphology designated as 'normal' at an IMSI-like magnification; (iv) the sperm classification; and (v) the criteria used to assess the outcome (e.g. clinical pregnancy and delivery rates per couple, per transfer or per cycle).

Hence, the objective of the present literature review was to assess the outcomes for IMSI vs. ICSI and determine the clinical situations in which the use of this assisted reproduction technology is likely to be of greatest value.

Materials and methods

This work performed a systematic review of the relevant literature, according to the PRISMA guidelines (Moher et al., 2009). The PubMed database was searched for work published between 2001 and March 2013 with the following search terms: 'IMSI', 'MSOME' and 'high-magnification, sperm'. The publications' titles, abstracts and reference lists were viewed and only relevant publications (i.e. those reporting on IMSI outcomes in terms of blastocyst, pregnancy, delivery and/or live birth rates) in English were selected and included. This review examined, compared and discussed study methodologies and results, including patient characteristics, the magnifications used for IMSI and ICSI (when stated) and the pregnancy and/or delivery rates associated with IMSI and ICSI. The results were subdivided into currently accepted indications of IMSI (i.e. clinically relevant indications confirmed by several studies, including at least two randomized clinical trials with a large sample size) and potential indications (i.e. those requiring additional research).

Results and discussion

Literature retrieved

The PubMed search identified a total of 168 publications (58 using the term 'IMSI', 28 using the term 'MSOME' and 82 using the terms 'high-magnification, sperm') indexed between 2001 and March 2013. After viewing the publications' titles, abstracts and reference lists, 24 studies which directly compared IMSI and ICSI were retrieved. Following the exclusion of two publications not written in English, a total of 22 studies were included in this review.

Indication for IMSI

In most studies, ICSI was indicated because of the presence of at least one male factor for infertility (oligo- and/or astheno- and/or teratozoospermia) (see, for example, Table 1). The indication of ICSI was not specified in three studies and varied in one other study. The only confirmed indication of IMSI is recurrent implantation failure following ICSI.

Outcomes after IMSI

The outcomes of IMSI following ICSI failure are summarized in Table 1.

In two studies, IMSI was directly compared with ICSI in couples matched for the number of previous ICSI failures (Bartoov et al., 2003; Oliveira et al., 2011). Bartoov et al. studied a total of 100 couples with an mean (range) of 4.1 (2—8) previous ICSI failures. When compared with ICSI (performed at a magnification of ×200 or ×400, $n = 50$ couples), IMSI (with selection of normal spermatozoa with no more than one small vacuole occupying <4% of the sperm head area, $n = 50$ couples) yielded a significantly higher clinical pregnancy rate per couple (30% versus 66%, respectively,